It's Not Business as Usual
CB ER, 2002
Reorganization, PDUFA, MDUFMA, GMPs and Countering Terrorism

PDA Annual Meeting
New Orleans, LA

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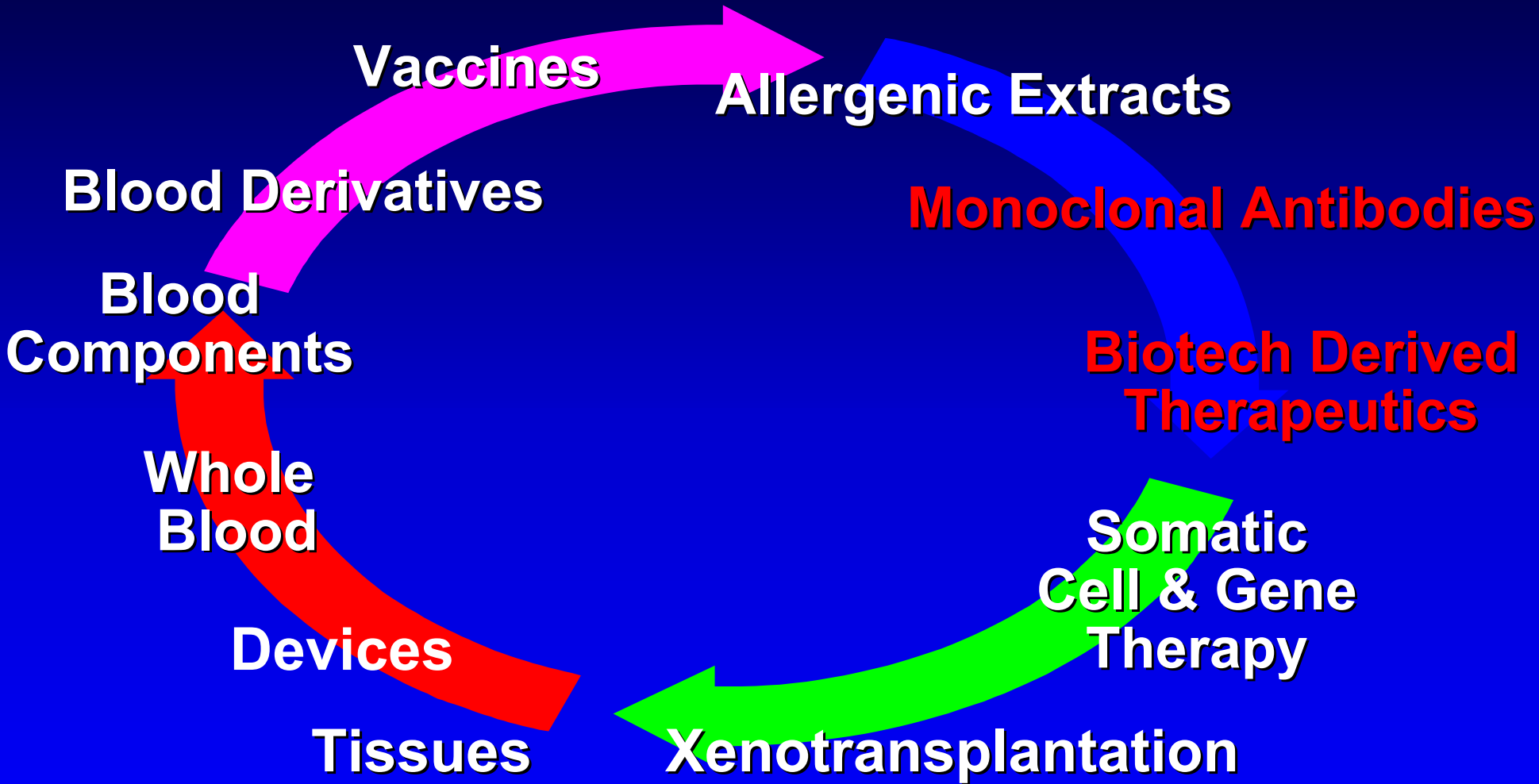
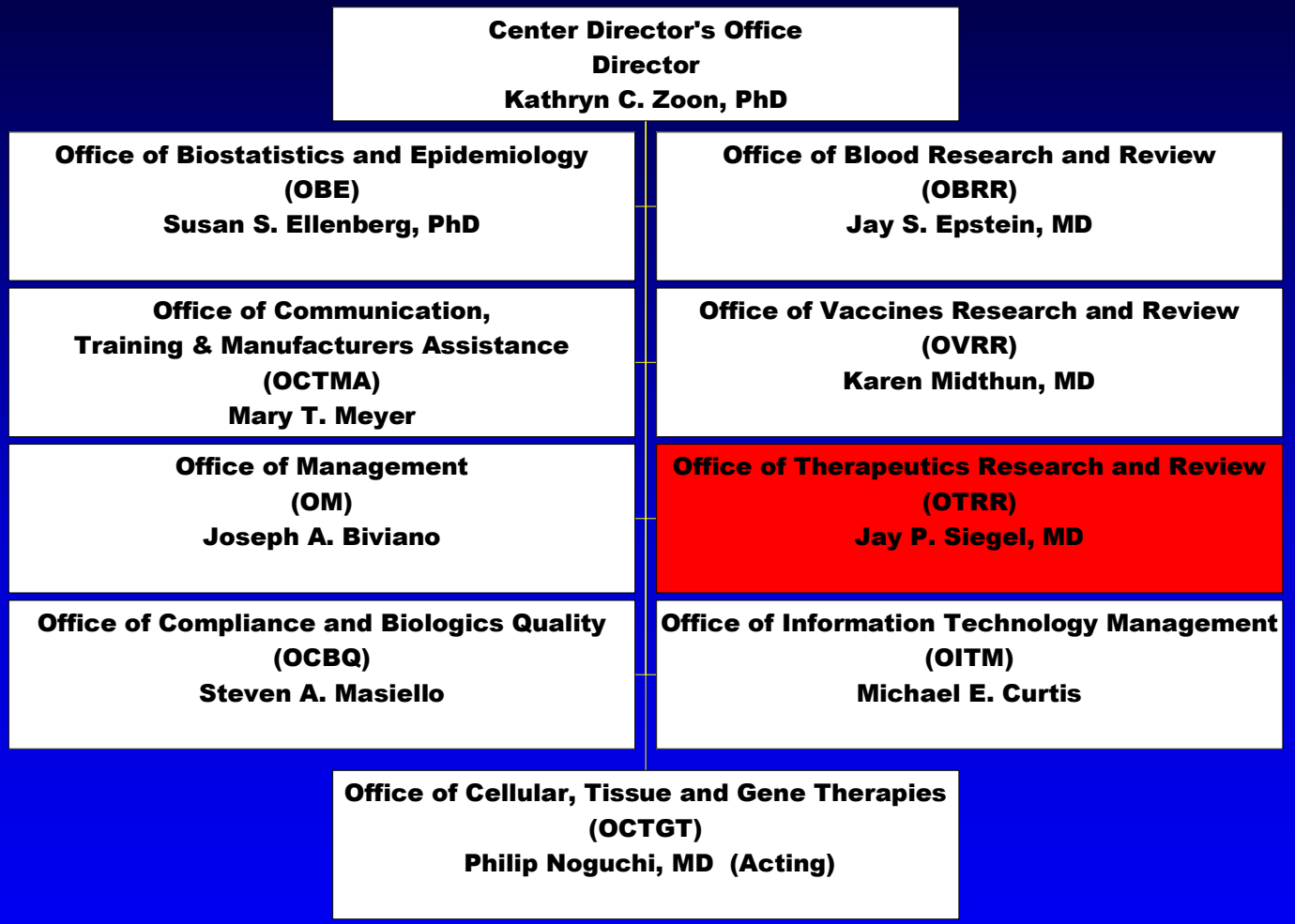
REORGANIZATION

BIOLOGICAL PRODUCTS REGULATED BY CBER



CBER Organization



C B
E R

What's Going

Monoclonal antibodies

Cytokines, growth factors, enzymes, interferons -- (including recombinant versions)

Proteins intended for therapeutic use that are extracted from animals or microorganisms

Other therapeutic immunotherapies

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What's Staying

- Monoclonal antibodies, cytokines, growth factors, or other proteins when used solely as an ex vivo constituent in a manufacturing process / when used solely as a reagent in the production of a product that is under the jurisdiction of CBER
- Viral-vectored gene insertions (i.e., "gene therapy")
- Products composed of human or animal cells or from physical parts of those cells

What's Staying (continued)

- Plasma expanders
- Allergen patch tests
- Allergenics
- Antitoxins, antivenins, and venoms
- In vitro diagnostics
- Vaccines
- Toxoids and toxins intended for immunization

PDUFA

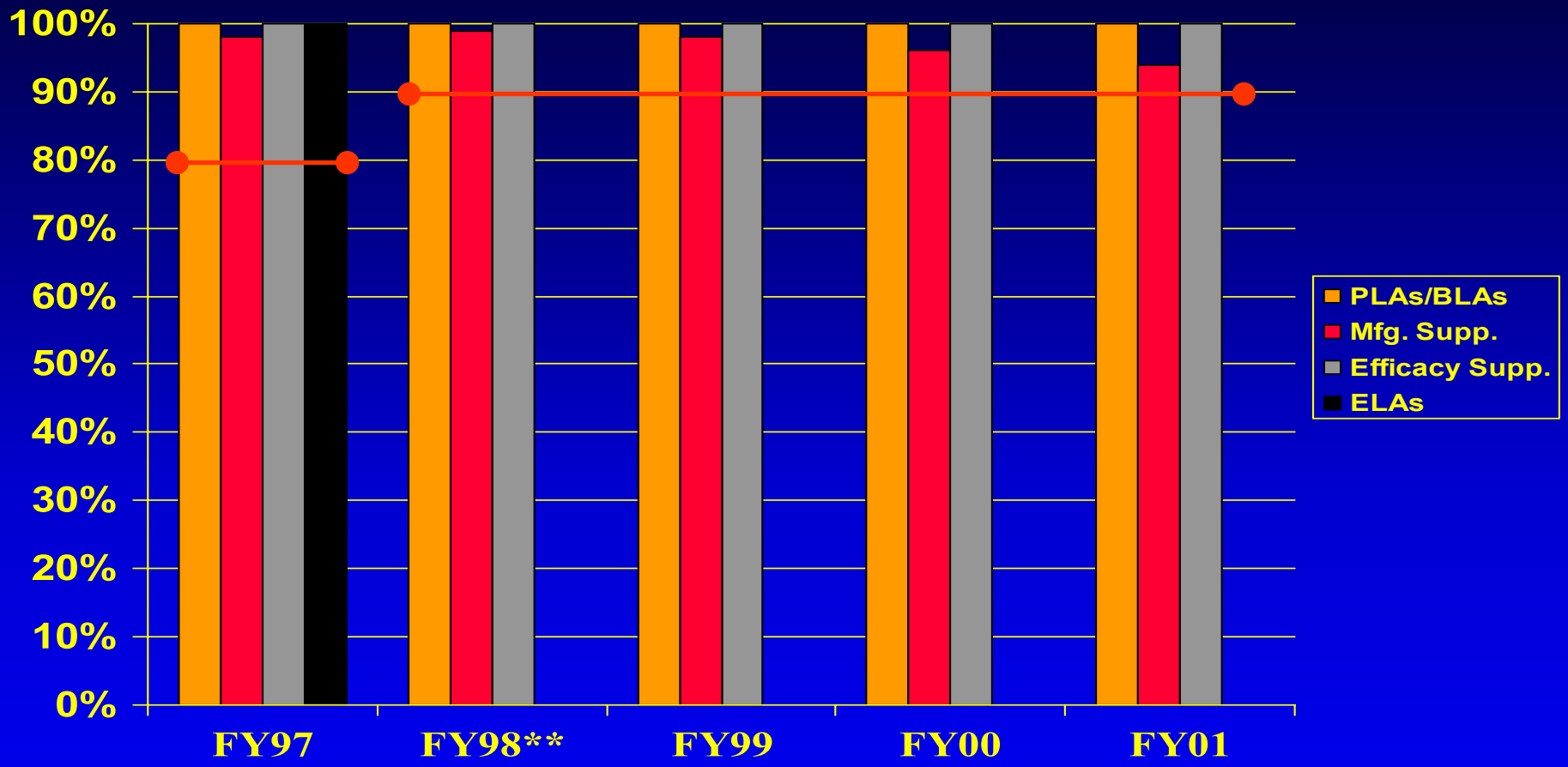
The OTRR, CBER record

- Science-based regulation of biologic therapeutics at OTRR has played a central role in the development and availability of safe and effective products of biotechnology that are revolutionizing medicine.
- OTRR scientists/physicians work independently of but closely with regulated biotechnology.
  - Extraordinary number of meetings
  - Timely, science based guidance
- OTRR scientists/physicians have provided international leadership in the science-based regulation of biotechnology products.

The OTRR, CBER record (continued)

- **The number of new product approvals is increasing.**
- **Despite the complexity and novelty of biotechnology products, review times and approval times compare favorably with those for other types of drugs.**
- **Biological therapeutics are often available first in the U.S.**
- **There has *never* been need to recall an OTRR-approved biotechnology drug due to safety concerns.**

CBER User Fee Review Performance
License Applications and Supplements
% of First Actions Within Goal*
By Cohort Fiscal Years 1997-2001



* PDUFA Performance Goals: FY97 - FY01=90% (Indicated by Red Lines)
** Beginning in FY98 ELAs were no longer included in PDUFA goals

Data through 30 Sep 02; FY 01 is not yet complete.

(253bp)RIMS 10/02/02

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CBER PDUFA II Procedural and Processing Goals Performance (as of October 31, 2002)

Regulatory Meetings Management										
			Actions Within Goal			Actions Overdue				
Fiscal Year	Goal	Meeting Requests Received	Completed	Pending	Total	Completed	Pending	Total	% Completed Within Goal[1]	*PDUFA Goal*
FY 1999	Response	387	283	0	283	104	0	104	73%	*70%*
	Held	364	321	0	321	43	0	43	88%	
	Minutes	328	282	0	282	46	0	46	86%	
FY 2000	Response	312	302	0	302	10	0	10	97%	*80%*
	Held	294	277	0	277	14	3	17	94%	
	Minutes	251	229	0	229	19	3	22	91%	
FY 2001	Response	281	275	0	275	6	0	6	98%	*90%*
	Held	246	218	21	239	6	1	7	97%	
	Minutes	180	157	20	177	3	0	3	98%	
FY 2002	Response	412	399	0	399	12	1	13	97%	*90%*
	Held	372	306	53	359	7	6	13	96%	
	Minutes	288	245	27	272	5	11	16	94%	

[1] - of those that have reached the goal date

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CBER PDUFA II Procedural and Processing Goals Performance – *cont.*
(as of October 31, 2002)

Special Protocol Assessment

Fiscal Year	Protocol Review Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal[1]	*PDUFA Goal*
		Completed	Pending	Total	Completed	Pending	Total		
FY 1999	0								*60%*
FY 2000	0								*70%*
FY 2001	1	1	0	1	0	0	0	100%	*80%*
FY 2002	4	4	0	4	0	0	0	100%	*90%*

Major Dispute Resolution

Fiscal Year	Dispute Resolution Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal[1]	*PDUFA Goal*
		Completed	Pending	Total	Completed	Pending	Total		
FY 1999	1	1	0	1	0	0	0	100%	*70%*
FY 2000	0								*80%*
FY 2001	2	2	0	2	0	0	0	100%	*90%*
FY 2002	4	4	0	4	0	0	0	100%	*90%*

Responses to Clinical Holds

Fiscal Year	Responses to Clinical Holds Received	Actions Within Goal			Actions Overdue			% Completed Within Goal[1]	*PDUFA Goal*
		Completed	Pending	Total	Completed	Pending	Total		
FY 1998	22	18	0	18	4	0	4	82%	*75%*
FY 1999	77	73	0	73	4	0	4	95%	*90%*
FY 2000	89	87	0	87	2	0	2	98%	*90%*
FY 2001	125	115	0	115	10	0	10	92%	*90%*
FY 2002	122	112	7	119	3	0	3	97%	*90%*

[1] - of those that have reached the goal date

Number of Cycles to Approval

- From CY 1995-2001, OTRR approved 41% of the original BLAs submitted within 1 cycle
- 19% took 3 or more cycles
- Numbers are comparable to NMEs approved during this same time period

Number of Approvals Within 12 Months

- CY 1996-2000, 14 of 22 BLAs submitted to OTRR approved within 12 months (64%)
- 13 were priority review; 10 within 12 months
- 9 were standard review; 4 approved within 12 months

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OTRR Meeting Goal Performance Under PDUFA II

- **Response to Meeting Requests: 99% within goal**
- **Meetings Held: 99% within goal**
- **Meeting Minutes: 99% within goal**
- **Non-PDUFA Products: 97%, 97% and 94%, respectively**

Source: FY 2001 Report to Congress

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PERFORMANCE GOALS
PDUFA II vs. PDUFA III

- **Original NDA/BLA Submissions: No Change**
- **Original NDA/BLA Resubmissions: No Change**
- **Original Efficacy Supplements: No Change**
- **Resubmitted Efficacy Supplements: Modified**
- **Original Manufacturing Supplements: No Change**
- **New Molecular Entity (NME): No Change**
- **Clinical Holds: No Change**
- **Major Dispute Resolution: No Change**
- **Special Protocol Question : No Change**

Meeting Management: Technical Change

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PDUFA III – NEW PROGRAMS

- **Continuous Marketing Application (CMA)**
- **Independent Consultants for Biotechnology Clinical trial Protocols**
- **Pre and Peri-NDA/BLA Risk Management Plan Activities**
- **First Cycle Review Performance Proposal**
- **Improving FDA Performance Management**
- **Electronic Applications and Submissions**

Electronic Submissions Goals

- Assist the reviewer community in meeting PDUFA review goals
- Provide reviewers with intuitive, standard presentations and tools to review electronic submissions effectively
- Provide the ability to manage all CBER submission types, starting with INDs, BLAs, and Promotional Labeling (current) with future functionality for 510(k)s and PMAs

Electronic Submissions Goals

- Establish electronic submissions standards and guidance for Industry
- Enable CBER to meet PDUFA and FDAMA electronic submissions mandates and timelines
- Decrease administrative processing time and costs of the submission process
- Enhance processes through electronic routing and secure transmission of information

Submission & Review Tools

- Electronic Document Room (EDR)
  - Provides the core system for CBER e-subs
- Electronic Secure Messaging (ESM)
  - Provides a secure communications channel between CBER and Industry
- Electronic Signature
  - Digital signatures compliant with 21 CFR Part 11
- E-Routing
  - Provides fully electronic workflow for routing

Status

- CBER is the first Center to accept fully electronic regulatory documents with digital signatures and automated submission and processing via ESM
- The EDR, ESM, and e-Routing are a complete, robust set of review tools to meet reviewer needs, developed in conjunction with the reviewer community
- CBER's electronic submission infrastructure and applications may form the core of an overall FDA electronic submission toolset
- The CBER Electronic Submissions program is robust and has made great strides since its inception in 1996

MDUFMA

Key Provisions of MDUFMA

- **Medical device user fees *and* additional appropriations.**
- **Third-party establishment inspections.**
- **Greater oversight of reprocessed single-use devices.**
- **Electronic labeling.**
- **Modular Review.**
- **FDA-OC oversight of combination products.**

Medical Device User Fees

- **Fees for PMAs, PDPs, BLAs, premarket reports (PMA for a reprocessed single-use device), certain supplements, 510(k)s.**
- **$25.1 million in fee revenues during FY 2003, rising to $35 million in FY 2007 (*plus* adjustments).**
- ***Plus* $15 million additional appropriations brings total new FDA resources to $40.1 million for FY 2003, rising to $50+ by 2007.**

User Fees (con't)

- First year fees range from $154,000 for a premarket application, to $2,187 for a 510(k).
- Reduced fees to protect small businesses. Small = sales and receipt $30,000,000 or less.
- Small business fees are 38% of standard fee, except for 510(k), which is 80%
- Small business fee for 510(k) starts FY 2004.
- Sunset October 1, 2007

GMPs

Pharmaceutical cGMPs for the 21st Century A Risk Based Approach

- Publicly announced on August 21, 2002
- Broadens/merges science-based risk management with an integrated quality systems approach
- Evaluation of approach to product quality regulation
- Includes human drugs, biological drugs, and veterinary drugs

First Goal

- Enhance focus of agency's cGMP requirements more squarely on potential risks to public health
- Provide additional regulatory attention and agency resources on those aspects of manufacturing that pose greatest potential risk

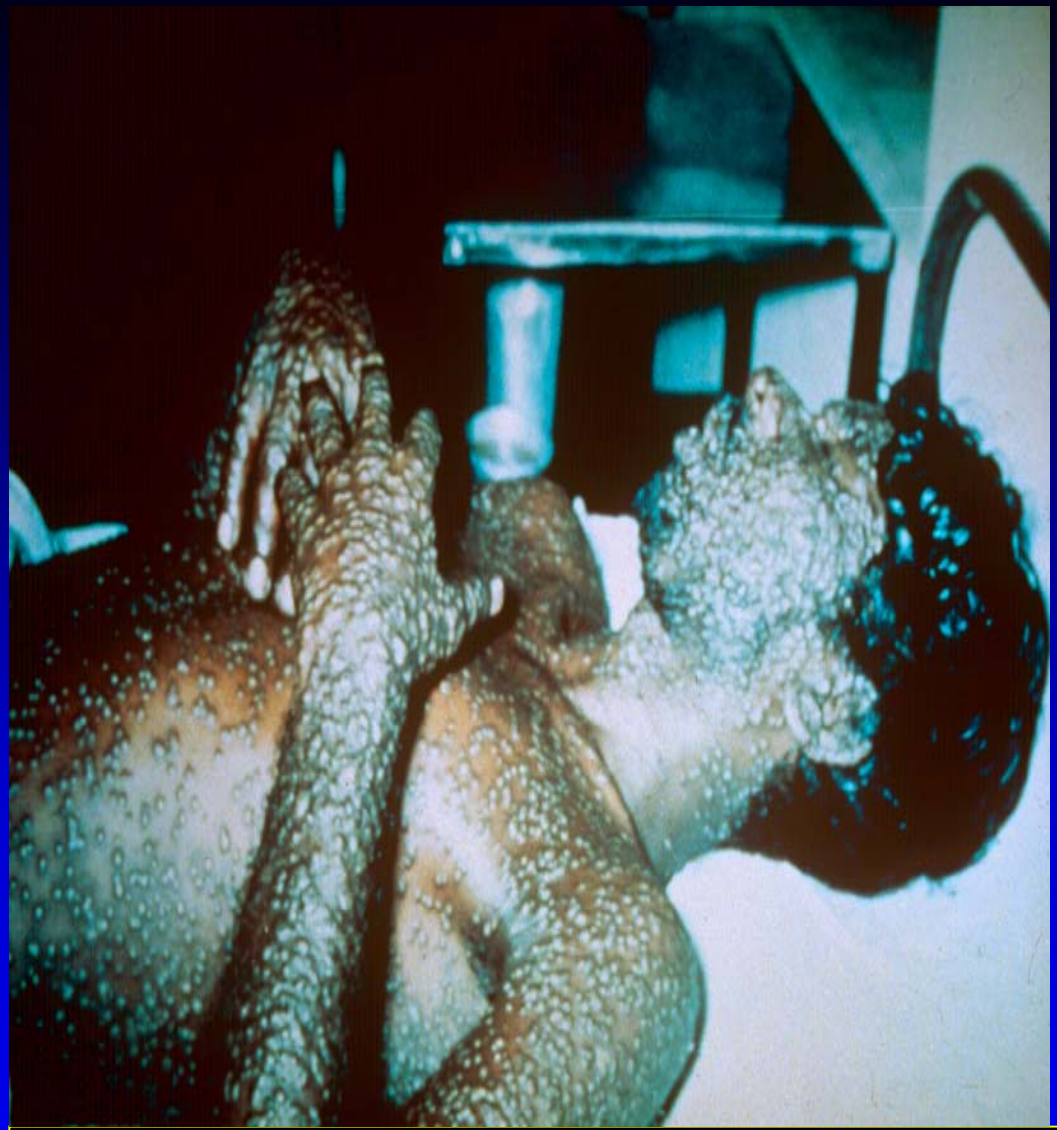
Second Goal

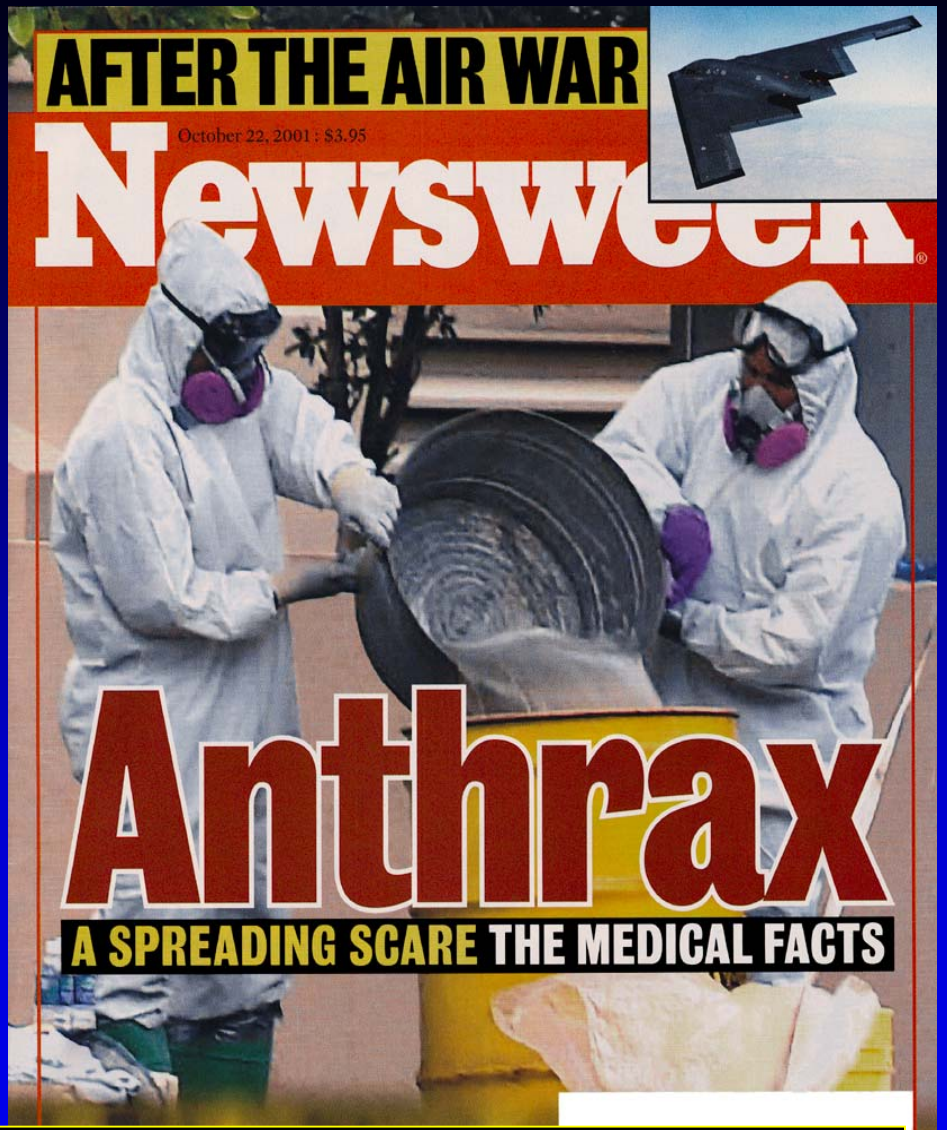
- **Help ensure that FDA's establishment and enforcement of pharmaceutical product quality standards does not impede innovation and introduction of new manufacturing technologies in the pharmaceutical industry**

Third Goal

- **Enhance consistency and predictability of FDA's approach to assuring production quality and safety among FDA Centers and field components**

COUNTERING TERRORISM





COUNTER- BIOTERRORISM

Countering Bioterrorism
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- Facilitate the availability of necessary medical products
- Scientific infrastructure to ensure availability of approved medical products
- Ensure availability of specialized equipment and facilities for containment
- Establish and disseminate the necessary guidance/standards

Key Actions
CBER

- Expedite development and licensure of new vaccines for anthrax, smallpox, and associated VIG
- Develop new approaches to approve medical products for countering bioterrorism
- Continue activities related to stockpile and product shortages
- Participate in numerous collaborative activities with other government agencies

HOW TO GET INFORMATION FROM CBER

Send E-MAIL to:

"CBER_INFO@CBER.FDA.GOV"

"OCTMA@CBER.FDA.GOV"

To visit CBER's Home page:

"www.fda.gov/cber"